REMARKS

The present specification describes (on page 2, lines 19-27 of the English language translation) that transvaginal absorption property of vitamin D, A and E, which as fat-soluble vitamins, is generally low but that applicants have found that some specific Vitamin Ds unexpectedly have an excellent transvaginal absorption property. As examples of such a vitamin D, 1α-hydroxyvitamin D_3 and 1, 25-dihydroxyvitamin D_3 are described in claim 5 and effects of these vitamin D_3s are corroborated in Example 1 and Comparative Example 1. The specification describes on page 10, lines 10-18 of the English language translation that:

> "Comparison and contemplation between the result of the present Comparative Example 1 and the result of the above Example 1 demonstrate that 1α-VD_3 in Example 1 is absorbed from the vaginal wall into the body by the intravaginal administration of 1α-VD_3 and quickly converted to 1,25-$(OH)_2D_3$, thereby affecting Ca metabolism, whereas no evidence that the administered drugs were absorbed from the vaginal wall was confirmed in the intravaginal administration of VitAD_3E in Comparative Example 1."

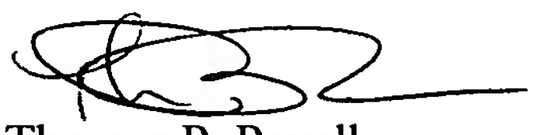
Thus, as described in the "Industrial Applicability" paragraph, the present invention has enabled advantageous use of transvaginal administration of the Vitamin D, according to the unexpected absorbability. In a case of transvaginally administering 1, 25-dihydroxyvitamin D_3, an advantage, which cannot be expected in a case of dose-dependent peroral administration, can be enjoyed. In this regard, the specification describes on page 20, line 31 to page 21 line 9 that:

> "Although it is known that a proportional rise in the AUC (area under the plasma concentration-time curve) of calcitriol in serum with an increase in a dose was not observed in oral administration (report by Muindi et al. (2002); *Pharmacokinetics of high-dose oral calcitriol: Results from a phase I trial of calcitriol and paclitaxel*; Clin. Pharmacol. Ther. 72: 648-659), the present result indicates that 1,25-$(OH)_2D_3$ is dose-dependently absorbed from the vaginal wall, so that the superiority of the vaginal administration of 1,25-$(OH)_2D_3$ is clear in this regard."

This description provides comparison between transvaginal administration and peroral administration, which is required by the Examiner in the Office Action.

Therefore, it can be concluded that the present invention would not have been obvious in light of the cited references, based on the fact that the present invention has unexpected effect in transvaginal administration of vitamin D_3 derivative as specified in the specification.

Respectfully submitted,



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